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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/771,895	02/04/2004	Rory F. Finn	32152	4167

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PHARMACIA CORPORATION
GLOBAL PATENT DEPARTMENT
POST OFFICE BOX 1027
ST. LOUIS, MO 63006

EXAMINER	
AUDET, MAURY A	
ART UNIT	**PAPER NUMBER**
1654	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/28/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/771,895	FINN, RORY F.	
	Examiner	Art Unit	
	Maury Audet	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/15/07*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *9 and 10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02/04/2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/15/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response and amendments of 3/14/07 is acknowledged. The new prior art of reference provided by IDS and explained in the arguments has prompted the 112 1st scope of enablement rejection to dropped and a new rejection under 103 necessary, made FINAL. Claims 1-8 remaining examined on the merits and 9-10 withdrawn from consideration.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rockich et al. (Research Report presented at the annual meeting of the American Association of Pharmaceutical Scientists, Boston, MA, 1432-1436, 1997 (cited in IDS and response 3/15/07)) and Hitoshi et al., (Brain Injury, Vol. 14, No. 7, 669-676, 2000 (cited in IDS and response 3/15/07)).

Applicant's response of 3/15/07 fully describe the relevant teachings of both Rockick et al. Hitoshi et al.. Both references teach the use of recombinant or native hGH to "treat", with some degree of "beneficial" result, traumatic brain syndrome (TBI).

> "The prior art also discloses *the use of hGH in treating traumatic brain injury* (Rockich et al. Pharmacotherapy (1999), 19:1432-6 Effect of recombinant human growth hormone and insulin-like growth factor-1 administration on IGF-1 and IGF-binding protein-3 levels in brain injury-submitted herewith in a Supplemental IDS). Rockich et al. concludes "infusion of rhlGF- 1 in conjunction with rhGH effectively achieved and maintained supraphysiologic IGF- 1 plasma concentrations throughout the dosing period in patients with TBI." (Abstract p 1432). Yamamura [Hitoshi] et al. evaluated the safety of GH in head trauma patients, by investigating *whether GH affects brain oedema caused by brain injury*, using a rat freeze-injury model (Brian Injury 14: 669-76, 2000, Effect of growth hormone on brain oedema caused by a cryogenic brain injury model in rats submitted herewith in a Supplemental IDS). [ ] Therefore, contrary to the Examiner's allegation the connection between traumatic brain injury and subarachnoid hemorrhage and hGH was well established in the art."

The only difference between the prior art and the claims at issue appears to be the use of a pegylated form of hGH (Applicant's formula I) rather than a recombinant or native form of hGH as in the references? And whether it would have been obvious to select the former in place of the latter?

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use any native or modified hGH, e.g. recombinant, pegylated, in the methods of treating traumatic brain syndrome (TBI; or related subarachnoid haemorrhage) of either Rockich et al. or Hitoshi et al., because the references advantageously teach that mere recombinant and native hGH "treat" TBI with "some beneficial", and the same and more would be expected of pegylated hGh since it is well known in the art that pegylation of proteins provides the advantages of both 1) protection from degradation (breakdown/cleavage) *in vivo* of said protein; and 2) longer duration of action therefrom (see e.g. examples of the known benefits

of pegylating proteins, even specifically hGH, in "Prior Art Made of Record but Not Relied Upon" below). The selection of ANY known hGH, including pegylated (like that of Applicant's formula I), for the reasons set for above, at the time of the invention for "treating" TBI with some "benefit" would have been merely a matter of routine optimization by one of ordinary skill in the art, depending on the cost/access to said form of hGH and the desired outcome of treatment (e.g. longer duration form). Absent evidence to the contrary of some unexpected result via a specific form of hGH, such as pegylated, *IN THIS SPECIFIC METHOD*, which has not been argued by Applicant or found via specification description/test or evidence in another form.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claim Rejections - 35 U.S.C. § 112 1st Scope

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

II. Treatment

In specific regards to the rejection of claims 1-8 under 112 1st scope of enablement, the latter has been dropped on the basis of references not previously of record which Applicant's

have shown "reasonably correlate[e]" (MPEP 2107.03) the invention is enabled for the present method of using an hGH to treat (in any way potentially beneficial – as the latter is not distinctly claimed) TBI and subarachnoid haemorrhage. [Scope over I. Prevention dropped based on amendment].

MPEP 2107.03 recites:

As a general matter, evidence of pharmacological or other biological activity of a compound will be relevant to an asserted therapeutic use if there is a reasonable correlation between the activity in question and the asserted utility. Cross v. Lizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985); In re Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980); Nelson v. Bowler, 626 F.2d 853, 206 USPQ 881 (CCPA 1980). An applicant can establish this reasonable correlation by relying on statistically relevant data documenting the activity of a compound or composition, arguments or reasoning, documentary evidence (e.g., articles in scientific journals), or any combination thereof. The applicant does not have to prove that a correlation exists between a particular activity and an asserted therapeutic use of a compound as a matter of statistical certainty, nor does he or she have to provide actual evidence of success in treating humans where such a utility is asserted. Instead, as the courts have repeatedly held, all that is required is a reasonable correlation between the activity and the asserted use. Nelson v. Bowler, 626 F.2d 853, 857, 206 USPQ 881, 884 (CCPA 1980).

In fact, the references provided above "reasonably correlate[ed]" the invention to the level of rendering obvious the presently claimed invention, as discussed above.

Prior Art Made of Record and Not Relied Upon

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

The following references are cited merely by example of modified hGH's, specifically pegylated hGH's to prevent said protein degradation/longer duration of action; well known in the

art since at least the early 90's as modified hGH's open to selection for use by artisans (pharmacists/doctors) administering hGH therapy:

WO 93/00109 (07.01.93) pages 2-4, pegylating hGH for the advantages of longer duration and decreased breakdown/loss of the injected form.

Clark et al. (J Biol Chem. 1996 Sep 6;271(36):21969-77 (abstract)) on "Long-acting growth hormones produced by conjugation with polyethylene glycol", specifically pegylated hGH as means for increasing the duration of activity as motivation for overriding any loss in receptor binding.

Conclusion

Applicant's submission of an information disclosure statement (and references therein) under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on 3/15/07 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609.04(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maury Audet whose telephone number is 571-272-0960. The examiner can normally be reached on M-Th. 7AM-5:30PM (10 Hrs.).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MA, 03/25/2007

Cecilia J. Tsang
Supervisory Patent Examiner
Technology Center 1600